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PULMONARY FUNCTION IN SMOKERS AND NONSMOKERS AT ALTITUDE

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PULMONARY FUNCTION IN SMOKERS AND NONSMOKERS AT ALTITUDE

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Human subjects participated in this study after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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FOREWORD

A task force (Fuertes Caminos, FC-90) of approximately 450 U.S. Army and Marine personnel was exposed to altitudes ranging from 3500 to 4050 m. This group of engineers and roadbuilders worked for nearly 5 months to build an extension to an airfield on the Andean altiplano in the vicinity of Potosi, Bolivia. Major elements of the FC-90 group were stationed at Fort Riley, KS, and represented the largest commitment of U.S. troops ever exposed to such high altitudes during peacetime or war. The mission objectives were no different from those which could be given to a similar task force under sea-level conditions.

The overall study examined the incidence and severity of altitude-related illnesses, decrements in physical performance, and changes in dietary habits. Results of pulmonary function testing conducted at Fort Riley and after deployment to Bolivia are presented in this report.

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EXECUTIVE SUMMARY

The study was conducted to determine if smoking cigarettes had any effect on pulmonary function at sea level (SL) or high altitude (HA) in young, healthy men. The design involved an initial pulmonary function testing (PFT) at two intervals approximately 5 days apart at SL and again at HA. A subset of the task force population consisting of 23 volunteers was tested at sea level and at HA. Smokers were defined as individuals who smoked greater than one pack/day for 3 years or more.

Forced vital capacity (FVC, L), forced expired volume in one second (FEV_1, L) and one-half second ($FEV_{0.5}$, L), peak expiratory flow (PEF, L/sec) and mid-expiratory flow (FEF_{25-75}, L/sec) were compared between 14 male smokers (S, mean ± SEM; 1.2 ± 0.2 pack/day, for 8.1 ± 1 yr; age 25.1 ± 1.3 yr), and 9 male nonsmokers (non-S, age 27.9 ± 2.8 yr) at Fort Riley, KS, barometric pressure P_B=720 torr (baseline), and within the first 5 days of arrival in Potosi, Bolivia (3540 m, P_B=505 torr). Relative to baseline values, FVC and FEV_1 were unchanged at HA in both S and non-S. $FEV_{0.5}$ increased 12.9% in non-S (2.7 ± 0.1 L to 3.1 ± 0.1 L, $p<0.05$), but were not changed in S. FEV_1/FVC ratio (a measure used to assess pulmonary obstruction) increased 5.6% in S (79.3 ± 0.3% to 84 ± 1.6%, $p<0.05$), but not in non-S. PEF increased 28.2% in S (8.4 ± 0.5 L/sec to 11.7 ± 0.8 L/sec, $p<0.002$), but not in non-S. Mid-expiratory flow (FEF_{25-75}) increased 22.4% in S (4.5 ± 0.3 L/sec to 5.8 ± 0.3 L/sec, $p<0.005$), but not in non-S. The significant increases in $FEV_{0.5}$ in non-S, and the increases in PEF, FEF_{25-75} and FEV_1/FVC ratio in S from baseline to HA may be explained by the decrease in air density/reduced airway resistance. This was not seen in FEV_1 (also a density influenced measurement) in either non-S or S. Although there were statistically significant differences in some of the respiratory variables, we concluded that these were of nominal importance and that a physiological difference between smokers and nonsmokers was not present.

INTRODUCTION

Pulmonary function has been measured frequently at sea level (SL) and in a few studies at high altitude (HA), (6-12,13,16,17) for a variety of clinical purposes. Quantitative pulmonary function tests, such as forced vital capacity (FVC) and forced expired volumes (FEV), are used to evaluate the status of the respiratory system and can typically determine mechanical impairment of this system due to respiratory insults such as smoking and a variety of other airborne pollutants. Impairment of pulmonary function due to smoking cigarettes is gradual and usually evident only in the latter stages of chronic obstructive pulmonary disease. However, cigarette smoking has been reported to cause a small but noticeable change or loss of pulmonary function early in the life of a smoker even before the disease state manifests itself (16). Smokers may experience aggravated problems initially caused by the hypoxia of altitude. Tobacco-induced problems such as hyperactive airways, increased mucous production (congested airways) and vascular changes due to nicotine can be aggravated by an increase in carboxyhemoglobin (impaired O_2 binding) and a reduction in forced vital capacity (3,5).

In previous studies, FVC has been shown to decrease upon ascent to HA (6,7,8,11,17,18). However, the decrease in air density at HA reduces airflow resistance, and this factor may offset any smoking-induced deficiencies in the younger smoking populations. A study by Wagner et al. (19) studied the effects of carbon monoxide (CO) in cigarette smoke and exercise at SL and hypobaric hypoxia. They reported that smokers have a blunted response to CO at HA and significant changes in their cardiovascular systems in both environments (19). In most studies of pulmonary function at SL or HA, either smokers were excluded or smoking status was not evaluated. The possible interactions of smoking and altitude on pulmonary function have not been reported previously.

It was hypothesized that pulmonary function would be more affected by HA of 3540 m in young, healthy smokers than in a group of similar nonsmokers. It was important to conduct this study because there are military operations in HA environments; for example, the Indian-Pakistan border war and the Indian-Chinese confrontation. There are also a large number of recreational activities in altitude environments all over the world (climbing to the summits of Mount McKinley and Mount Everest, as some examples). Whether military or civilian, individuals involved in these activities represent a wide variety of lifestyles and levels of fitness. In addition, a large segment of the general population (~26%) smoke cigarettes in excess of one pack/day (16). The largest growing segment of smokers is below 30 years of age. The lungs of young smokers may undergo changes such as pulmonary congestion and a decreased affinity for O_2 due to increased blood carboxyhemoglobin levels. These changes may pose an increased risk of acute mountain sickness symptoms or delayed acclimatization at HA. Other factors affecting acclimatization that were observed with smokers were a decreased sensitivity to hypoxia, as well as a lower hypoxic ventilatory response (19). The objectives of this study were to compare the pulmonary function of smokers with that of nonsmokers and to study the effect of short-term residence at HA.

METHODS

STUDY BACKGROUND

Four hundred and fifty Army and Marine participants of FC-90 (a joint American/Bolivian goodwill construction project) were medically evaluated and cleared by physicians prior to inclusion in the construction project. Of these, a sample of approximately 100 males were pre-selected by the task force commander to participate

in studies conducted by the Altitude Physiology and Medicine Division and the Military Nutrition Division of the U.S. Army Research Institute of Environmental Medicine, Natick, MA.

STUDY DESIGN

The study was divided into two testing phases: A pre-altitude deployment phase conducted over a two-week period at Fort Riley, KS (P_B=720 torr, 460 m, baseline), and an altitude phase conducted over a five-day period on a plateau in Santa Lucia, Bolivia, (P_B= 505 torr, 3540 m).

Subjects

Eighty unacclimatized, young, healthy soldiers were evaluated at baseline altitude. Individuals were classified as smokers (n=40, individuals who smoked greater than one pack/day for 3 years or more), or nonsmokers (n=40) based upon their responses to a smoking history questionnaire. All subjects were native to low altitudes (<500 m). They gave their voluntary and written informed consent to participate in this investigation.

These unacclimatized individuals were transported to La Paz, Bolivia, by aircraft and then spent 40 hours on a train traveling to the plateau area of Santa Lucia (9). After several days on the plateau, only 23 individuals (14 smokers and 9 nonsmokers) completed all the tests including repeated measures. The study design required at least two measurements: one during the first 3 days (to determine if acclimatization would affect the pulmonary measurements) and a second test ~7 days later to eliminate any training effect. Table 1 summarizes the general physical characteristics of the subjects.

Spirometry tests

Pulmonary function testing was performed using a Collins Model 421 Survey Spirometer (Braintree, MA), with subjects in a standing position. Subjects were coached during all trials, and the best three to five trials were recorded on each of the test days. Tests were considered acceptable if they met standards set by the American Thoracic Society (1,2).

Pulmonary function tests consisted of a timed forced vital capacity (FVC) and FEV_1 and $FEV_{0.5}$ measurements, the latter two tests are the volumes of air within the lungs expelled during one second and one-half second of a forced expiration. The latter two parameters are also measurements used to assess air flow limitations. Mid-forced expiratory flow (FEF_{25-75}) and peak expiratory flow (PEF) were also measured. The ratio of FEV_1/FVC was calculated.

All volumes were corrected to barometric temperature and pressure saturated (BTPS). Laboratory temperatures were maintained at ~23°C (range 21.5° to 24.5°C) at baseline and ~20.3°C (range 18.5° to 21.3°C) at HA. The highest value of pulmonary function from each of the three trials was selected for subsequent analysis. The single highest measure for each variable was then used for comparison with predicted values (4,15). The percentage predicted for all measured variables was calculated for a larger baseline SL population (n=80, Table 2), as well as for the smaller group (n=23) that completed the HA phase. The sea-level data were analyzed for within group differences and smoking, whereas the other subgroup's data were analyzed for statistical significance using two-way analysis of variance (smoking, altitude) with repeated measures in both variables.

RESULTS

There were no differences between smokers and nonsmokers in any of the measured variables in the larger baseline population (n=80, 40/group) (Table 2).

In the subgroup (n=23), there were significant increases in PEF, FEF_{25-75}, and FEV_1/FVC ratio in S, as well as $FEV_{0.5}$ in non-S from baseline to HA. There were significant increases in PEF (8.8 ± 1.0 L/sec and 11.7 ± 0.8 L/sec, $p<0.05$) and FEF_{25-75} (4.5 ± 0.4 L/sec and 5.8 ± 0.3 L/sec, $p<0.05$) in nonsmokers and smokers, respectively, at HA. There was also a significant difference (18.9%) in $FEV_{0.5}$ between nonsmokers and smokers at baseline (2.7 ± 0.1 L/sec and 3.2 ± 0.1 L/sec, $p>0.05$, 15.6%), but not at HA.

In the smokers (n=14), FVC, FEV_1, and $FEV_{0.5}$ were not significantly different between baseline and high altitude (Table 3). The FEV_1/FVC ratio was significantly increased (79.3 ± 0.3% to 84 ± 1.6%, $p<0.05$, 5.6%). The peak (PEF) and mid-expiratory flows (FEF_{25-75}) were significantly increased in smokers (8.4 ± 0.5 L/sec to 11.7 ± 0.8 L/sec, $p<0.002$, 28.2%) and (4.5 ± 0.3 L/sec to 5.8 ± 0.3 L/sec, $p<0.005$, 22.4%, respectively).

In nonsmokers (n=9), FVC, FEV_1, FEV_1/FVC ratio, FEF_{25-75} and PEF measurements were not significantly different between baseline and HA. The $FEV_{0.5}$, was increased 12.9% from baseline (2.7 ± 0.1 L to 3.1 ± 0.1 L, $p<0.05$).

DISCUSSION

It is possible that if the total group of soldiers tested at Fort Riley (n=80) were retested at 3540 m, the results might be different. However, a power analysis was used to provide information regarding the negative findings from standard statistical evaluations. The results of this statistical test revealed that the sample size was too

small to detect a significant difference (required sample size needed for pulmonary volume measurements was >120 subjects and for flow measurements required >85 subjects). The powers for this study ranged from 3% to 17%. The chance of detecting a difference in FVC was less than 5% between baseline and HA in smokers. In a similar comparison with FEV_1 it was less than 10% and for FEF_{25-75} there was less than a 17% chance in nonsmokers.

Since there is little known about relatively young, healthy smokers at SL or HA (individuals under 30, having smoked less than 10 years, and having a consumption rate of less than 2 packs/day), we decided to use standard pulmonary function tests to evaluate the mechanical status and general physiology of the respiratory system.

In one report at 2500 m (2), smokers had a slightly larger FVC and a smaller FEV_1 than their nonsmoking counterparts and a significant reduction in the FVC\FEV_1 ratio between baseline and HA. Thus, it is possible that these smokers could have smaller but more consistent changes in FVC and FEV_1 than nonsmokers at HA. In the current study, there was no significant change in FVC in both groups at HA. In smokers, the FEV_1 was slightly higher from baseline values than nonsmokers (6.8%, ns). Ironically, this apparent increase in FEV_1 measurement from baseline occurred in both groups at 3540 m, and the change in FEV_1 is only slightly smaller than the significant increase of 7.1% in nonsmokers at 4300 m, which was observed in an earlier study (6-8).

The smokers had a two-fold change in FEF_{25-75} from baseline (22.4% vs. 11.1%) and had a larger percentage change from baseline in PEF than the nonsmokers (28.2% vs. 11.4%). Although the changes in smokers are not physiologically sufficient to create physical limitations at HA, there are large differences in our flow measurements that are consistent with data reported by others (2,16). In this study at 3540 m, one may expect the lack of significant differences in the majority of pulmonary parameters in the smokers is due to the decrease in gas density (at P_B =505 or 34% of SL pressure) as compared to the density difference at 4300 m, or that the population studied was too small. We believe that it is more likely that significant changes have not occurred in this group because they have not smoked cigarettes for a long period

of time. One recent study has determined a respiratory volume loss of 10 ml/year/pack of cigarettes smoked (12). This volume is very small and requires many years to significantly impact respiratory function.

Interpretations of the flow data indicate that smokers are undergoing small changes in compliance that are not seen in a control group of nonsmokers, thus affecting flow characteristics in the lung (15). As gas density decreases with HA, greater inspiratory and expiratory flows are found with increased ventilation (6,7,8,18). The $FEV_{0.5}$ measurement offers the best interpretation of the mechanics of the lung and correlates well with data that indicate that older nonsmokers and young smokers (16) undergo compliance changes that are similar (i.e., reduced elasticity of the lung tissue). That is, as one gets older, the lungs become less compliant, and smoking cigarettes may induce changes in compliance of the lung more rapidly in young people who smoke cigarettes. This measure was the only consistently significant result seen in this study and may possibly indicate that some minor changes are occurring in the lung, but they cannot be related to smoking behavior only.

Several investigators (6,10,13,14,17) have found small decrements in FVC ranging from 2.4% to 3.1% at altitudes ranging from 3540 m to 5538 m with nonsmoking subjects. These investigators also reported increased FEV_1s, ranging from 4.2% to 6.8%. In addition, decrements in FVC have been shown at simulated altitudes with (hypobaric hypoxia) and without hypoxia (hypobaric normoxia); i.e., the change is not attributable to hypoxia alone, but is probably pressure related (18). In this study we observed similar percentages of increase in both groups, and smokers showed no differences in FEV_1 from baseline values in the same test environment, and nearly equal to what we saw earlier at 4300 m with 21 nonsmokers (7,8).

Our hypothesis that significant disadvantages would be observable in young smokers at HA was rejected. It is possible that an altitude of 3540 m was not severe enough, or the smoking history in this group was not of a sufficient magnitude to produce measurable differences.

CONCLUSIONS

The cigarette smoking status of these healthy, young men under either baseline or HA conditions did not influence pulmonary measurements such as FVC, FEV_1 or their ratio. Significant differences in $FEV_{0.5}$, FEF_{25-75} and PEF were probably due to the reduced density of air at 3540 meters. In all probability, if you are a healthy smoker at SL you are likely to be a healthy smoker at HA.

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Table 1

PHYSICAL CHARACTERISTICS OF THE TEST SUBJECTS

	ALL (n=23)	SMOKERS (n=14)	NONSMOKERS (n=9)
ALTITUDE PHASE			
AGE (yr)	25.8 ± 1.4	25.1 ± 1.3	27.9 ± 2.8
HEIGHT (cm)	175.5 ± 1.5	174.2 ± 1.8	177.8 ± 2.9
WEIGHT (kg)	81.2 ± 2.3	78.2 ± 2.3	85.8 ± 4.0
BASELINE PHASE			
	(n=80)	(n=40)	(n=40)
AGE (yr)	25.0 ± 0.8	25.1 ± 0.8	24.8 ± 0.9
HEIGHT (cm)	176 ± 1	175.3 ± 0.9	177 ± 1.2
WEIGHT (kg)	78.9 ± 1.5	78.7 ± 1.4	78.9 ± 1.7

Values are means ± S.E.M.

Table 2

LUNG VOLUME/FLOW MEASUREMENTS AT BASELINE

	NONSMOKERS		SMOKERS	
	Baseline	%pred	Baseline	%pred
FVC	5.1 ± 0.8	94	5.2 ± 0.8	98
FEV_1	3.9 ± 0.7	90	4.1 ± 0.6	95
FEV_1/FVC	76.7 ± 3.0	96	78.2 ± 6.4	97
PEF	8.1 ± 2.1	83	7.9 ± 1.8	83
FEF_{25-75}	4.1 ± 0.6	72	4.2 ± 0.9	76

Values are means ± S.E.M., n = 80; 40 per group.
%pred = % predicted of baseline value for each group.

Table 3

LUNG VOLUME/FLOW MEASUREMENTS

	NONSMOKERS				SMOKERS			
	Baseline	%pred	HA	%predHA	Baseline	%pred	HA	%predHA
FVC	5.2 ± 0.2	96	5.2 ± 0.2	97	5.3 ± 0.2	100	5.3 ± 0.2	100
FEV_1	3.9 ± 0.2	92	4.2 ± 0.2	99	4.1 ± 0.2	98	4.4 ± 0.2	104
FEV_1/FVC	75.9 ± 3.0	96	81.1 ± 3.0	102	79.3 ± 0.3	99	84 ± 1.6†	104
PEF	7.8 ± 0.6	79	8.8 ± 1.0	91	8.4 ± 0.5	89	11.7 ± 0.8†*	124
FEF_{25-75}	4.0 ± 0.3	72	4.5 ± 0.4	84	4.5 ± 0.3	83	5.8 ± 0.3†*	107
$FEV_{0.5}$	2.7 ± 0.1	-	3.1 ± 0.1†	-	3.2 ± 0.1*	-	3.4 ± 0.1	-

Values are means ± S.E.M., n = 9 and 14, respectively.

† Significantly different from baseline ($p<0.05$).

* Significantly different between nonsmokers and smokers ($p<0.05$).

% pred = % predicted of baseline value for each group.

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